REMARKS/ARGUMENTS

The invention in this application involves the provision of a standard diluent for use in detecting target analytes in an immunoassay, in which two or more different target analytes are to be detected in a multiplex (i.e., simultaneous) assay. In preferred versions, the assay is aimed at detecting up to fifty or 100 different target analytes, preferably from two to fifty, or three to twenty, or four to fifteen, and in one example, eight different target analytes. The standard diluent of a biological fluid that is of a type that normally contains all the target analytes to be detected but, as present in the assay kit, is substantially free of these analytes.

The standard diluent that is substantially free of these target analytes is prepared from the appropriate biological fluid in one of two ways. In one embodiment (see, for example, claim 2), the biological fluid initially contains the target analytes, but they are substantially removed, for example by affinity chromatography, to produce the standard diluent that is included in the kit. In the other embodiment, the biological fluid is obtained from a host (for example, a human) whose biological fluid is already substantially free of the desired target analytes.

As stated in the specification, the term "substantially free" means that the target analytes either are undetectable by immunoassay methods, or that they are detectable, but are present in an amount below a selected sensitivity threshold.

Such standard diluents make possible the multiplex analyses for a plurality of target analytes ranging upwards from two to one hundred, or some intermediate number, as described in the specification, which contains an example showing the use of a standard diluent according to the invention in a procedure for detection of eight target analytes.

Claims 1-31 and 49-60 are under examination in this application.

Applicants note the withdrawal of previous rejections under 35 U.S.C. 112. Currently claim 9 is rejected; it contains an artifact in the form of the number "1" after the period, which has now been removed by this amendment.

In preparing this amendment it was noticed that claims 49-54, drafted as being dependent on claim 1, began with the words "A standard diluent" whereas claim 1 is directed to a kit comprising a standard diluent. Claims 49-54 have been corrected in this regard. No difference in their meaning or scope is intended thereby

The previous rejection of Claims 1-3, 5-8, 11, 12 and 15-17 as anticipated by Tamarkin et al. has been withdrawn. The current Office Action now contains a rejection of these claims, together with claim 49, as obvious over the combination of Tamarkin et al. with Barrera et al.

Applicants respectfully controvert this rejection. As discussed in the previous amendment, and as accepted by the Examiner in withdrawing the rejection of these claims as anticipated by Tamarkin et al., this reference teaches the removal of only a single target analyte (IL-1 or IL-2) from a serum solution. Throughout the specification Tamarkin et al. refer to "a cytokine" and "the cytokine" but do not use the plural form. In column 16 (lines 37-42) Tamarkin et al. refer to preabsorption of IL-1 or IL-2 from a serum solution, but not of both. This statement is repeated at col. 17 lines 39-43. At col. 17 lines 14-22, parallel immunoassays are conducted for each of IL-1 and IL-2; note the term "both the IL-1 and IL-2 EIAs".

Barrera et al. is now cited as teaching removal of two cytokines (IL-1β and TNF) from a biological fluid to be used as diluent in cytokine assays, to provide for a matrix similar to the sample.

However, Barrera et al., like Tamarkin et al., prepare a standard diluent that is missing only a single analyte - not a plurality of analytes. See, for example, page 100, right hand column ("The blood compartment contained ^{125}I-labeled recombinant human IL-1β or TNF, while the plasma in the dialysate compartment did not contain radiolabeled cytokine." (emphasis added). All of the experimental work in this publication describes the use of dialysis to remove a single cytokine from a blood sample and compare the resulting specimen with the original. No removal of two or more cytokines or production of a sample lacking two or more cytokines was carried out. This reference does not add the missing factor to Tamarkin et al.

Claims 2, 4 and 50-53 are rejected as obvious over Tamarkin et al. and Barrera et al. in view of van Emon et al. The latter reference is cited for its disclosure of affinity chromatography to remove targets. However, as above, neither Tamarkin et al. nor Barrera et al. disclose working with multiple target analytes, and van Emon et al. do not make up for this deficiency.

Claim 9 is rejected as obvious over Tamarkin et al. and Barrera et al. combined with Brailly et al., which is cited as disclosing certain of the target analytes. Again, however, the rejection is not well founded as none of the references discloses working with multiple target analytes.

Claims 10, 18 and 19 are rejected as obvious over Tamarkin et al. and Barrera et al. in view of Posner et al. The latter reference is cited for teaching mixing of two or more different target analytes to prepare controls or calibrants. However, Posner et al. do not use materials where target analytes have been removed or are initially substantially not present. Relevance of Posner et al. is not seen to kits and the like such as those claimed. Additionally, Posner et al. are directed to controls, not to standard diluents.

Claims 13, 14, 20-23, 25-28, 30, 31 and 55 are rejected over Tamarkin et al. and Barrera et al. in combination with Chandler et al. Chandler et al. is directed to a series of differentiable beads. However, since Tamarkin et al. and Barrera et al. only disclose working with a single analyte, there would be no need for the use of differentiable beads in their processes.

Claims 24 and 56-59 are rejected over the combination of Tamarkin et al. and Barrera et al. with Posner et al. and van Emon et al. Claim 29 is rejected as obvious over Tamarkin et al. and Barrera et al. in combination with Posner et al. and Brailly. However, for reasons mentioned above, these combinations do not render claims 24 and 29 obvious.

Applicants note that claims 54 and 60 would be allowable if written in independent form. However, as discussed above, Applicants believe all of the claims under examination are allowable.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

Joel G. Ackerman
Reg. No. 24,307

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
Attachments
JA:ja
60392033 v1